

REMARKS

Claims 58, and 65 have been canceled. New claims 66 - 69 have been added. Claims 1, 3-19, 27, 29-34, 39-44, 52, 53, and 56 have been amended. The application includes claims 1, 3-27, 29-53, 56, 59, 60, 66- 69. Of these, claims 20-26 and 45-51 are withdrawn and are subject to rejoinder and new claims 67-69 are drawn to a composition in the non-elected species.

Based on the interview, new claims 66 - 69 have been added as greatly simplified compositions which are drawn to the compositions described in the patent specification and the concurrently filed declaration of David Anderson, and which were demonstrated at the interview.

As was discussed at the interview, the independent claims have been amended to follow a format similar to that presented in the corresponding granted European Patent 1 345 589. In particular, in independent claims 1 and 27, the components of the composition are designated as “A)” and “B)”. Furthermore, the independent claims 1, 27, 52, 53, and new claims 66 and 67 each now require that the compound be solubilized in the structured fluid which can contain either or both a reversed cubic liquid crystalline phase or a reversed hexagonal liquid crystalline phase.

As noted during the interview, the patent application describes the discovery of a “new” material composed of reversed cubic liquid crystalline phase or reversed hexagonal liquid crystalline phase structured fluid which includes a polar solvent, a lipid or surfactant, an essential oil or dissolution/solubilization agent with a compound solubilized in the structured fluid.

Constructing such materials and recognition that a material falls within the ambit of the claims, would be well recognized by one of skill in the art. As noted during the interview, and as set forth in the Declaration of Richard Templer filed June 7, 2007, one of ordinary skill in the art could readily produce the materials after reading the patent application. At item 11 of that declaration it is noted that

“Knowledge of specific percentage ranges of constituents is not required by one of ordinary skill in the art; and with would be know that such percentages would vary depending on the constituents being combined... one of ordinary skill in the art would have sufficient knowledge and training to easily deduce the constituents and ratios of constituents, based on the teachings in the application, to produce a composition or solvent system which is to include a structured fluid...one of ordinary skill in the art would be able, upon review of the...application, to produce a structured fluid having a reversed cubic phase or reversed hexagonal liquid crystalline phase from any of a number of polar solvents, lipids or surfactants, essential oils or dissolution/solubilization

agents...and to incorporate...any of a number of difficult to solubilize compound in the structured fluid”. (emphasis added)

As was discussed at the interview, the claims do not cover any collection of four constituents in any ratio. Rather, they cover only those combinations of constituents which yield reverse cubic phase or reversed hexagonal phase materials in which is solubilized the compound that is otherwise difficult to solubilize. As discussed in detail in the declaration of Dr. Templer, one of ordinary skill in the art could use the teachings set forth in the patent application and standard procedures to those of ordinary skill in the art, such as systematically creating a phase diagram of the specific chosen system to identify those regions representing compositions of the invention, to produce these materials in a matter of hours (see item 11).

To highlight the metes and bounds of the claimed invention, the claims have been re-cast in the manner similar to the corresponding European Patent 1 345, 589, and, in addition, as discussed at the interview, the proviso that “wherein said polar solvent, said lipid or surfactant, and said essential or dissolution/solubilization agent each have attributes and are present in amounts sufficient to form said structured fluid with said compound solubilized therein” has been added to claims 1 and 27. Dependent claims 14 and 39 specify that the lipid or surfactant that is a low HLB surfactant (as is discussed throughout the application), and new independent claims 66 – 68 now specify particular ingredients: phospholipid and water. In the printed publication of this application, paragraphs [0101]-[0104] describe water based reversed hexagonal liquid crystalline materials; paragraphs [0116]-[0118] describe water based reversed cubic liquid crystalline materials; paragraph [0204] discloses that the addition of alpha tocopherol to phospholipid /water systems induces a transition to a reversed hexagonal or reversed cubic liquid crystalline material; and paragraphs [0219]-[0213] describe mixing essential oils with phospholipid and water systems to produce reversed cubic and reversed hexagonal liquid crystalline materials with difficult to solubilize drugs, such as paclitaxel, solubilized therein.

In the office action, claims 1, 3-19, 27, 29-44, 52-53, 56, 58-60, and 65 were rejected as being obvious over U.S. Patent 5,531,925 to Landh in view of U.S. Patent 5,716,928 to Benet, and U.S. Patent 5,541,287 to Yau (as evidenced by The Merck Index). This rejection is traversed in view of the amendments above, and the evidence presented in the concurrently filed declaration of David Anderson.

As noted during the interview, experiments were performed by David Anderson with spearmint oil (selected in response to an election of species in the present application) and clove oil (selected in response to an election of species in USSN 10/460,659). David Anderson has previously provided a declaration in the present case on October 14, 2008, which identifies his expertise. The experiments clearly show that if Benet is combined with Landh, a reversed cubic liquid crystalline phase or a reversed hexagonal liquid crystalline phase **does not** result---rather the combination of the Benet essential oil with the Landh particle results in melting of the Landh particle. See particularly, items 4-7 of the declaration. In contrast, as shown in item 8 of the declaration of David Anderson a reversed cubic liquid crystalline phase material, as set forth in the claims (see claims 1, 27, 52, 53, and 67) results when spearmint oil, water and phosphatidylcholine are combined. Item 8, also shows this reverse cubic liquid crystalline phase can be repeated when tocopherol (Vitamin E), water and phosphatidylcholine are combined (see claims 1, 27, 52, 53, and 66).

U.S. Patent 5,531,925 to Landh describes a coated, three component drug carrying particle having an interior reverse cubic or reversed hexagonal phases: 1) polar solvent, 2) surfactant, and 3) drug. **Landh does not contain an essential oil, and the cubic or hexagonal phase material does not comprise a solubilizing fourth component**. Landh discusses using the particle to solubilize drugs that are difficult to solubilize (column 20, lines 3 et seq.), and creating and stabilizing the particle by using fragmentation agents (column 9, line 20) to disrupt a homogenous reversed cubic or hexagonal phase material (column 7, line 55; column 12, line 31) creating a separate, additional and distinct surface phase or coating. **A surface coating of a different phase of material is required to stabilize the Landh particles** (Claim 1 requires the surface phase to be distinct from the interior phase)

U.S. Patent 5,716,928 to Benet describes **co-administration** of drugs with essential oils to make the drugs more **bioavailable** (the amount of drug which is systemically available over time; see column 2, line 46), not by any interaction with the formulation but by inhibiting the pGp and CYP4a efflux mechanism in the cellular membranes in the body of the patient. **Benet does not describe solubilizing a drug with essential oils. Benet does not describe reverse cubic phase or reversed hexagonal phase materials. Benet does not teach formulation at all.**

The data presented at the interview and in the concurrently filed declaration demonstrate that simply **adding essential oils to Landh particles does not produce reverse cubic phase materials incorporating essential oils. Instead, essential oils tend to break down the Landh**

particles, as well as the reversed cubic and hexagonal phase materials of which they are comprised. Thus, even assuming it were obvious to combine Landh and Benet, once having done so it would have been immediately obvious to stop doing so. Similar results would be obtained if the cubic phase from Engstrom (U.S. Patent 5,151,272 cited in Landh and in the currently filed IDS and which was referenced in a co-pending application for this case---note that "Larsson" is the same joint-inventor for Landh and Engstrom) were used.

Yau has been relied upon for the use of gentisic acid and is discussed in detail in the previously filed amendment. As acknowledged by the Examiner, there is no showing in Yau that reversed cubic liquid crystalline phase or reversed hexagonal liquid crystalline phase particles can be formed when combined with polar solvents and lipids.

As discussed at the interview, merely combining different ingredients does not produce the claimed reversed cubic liquid crystalline phase or reversed hexagonal liquid crystalline phase materials. Item 9 of the declaration of David Anderson demonstrates that many different phases of thermodynamically stable nanostructured materials may form from the combination of the same ingredients in different ratios. Item 10 of the declaration of David Anderson demonstrates that a minimum amount of tocopherol is needed for a particular formulation of components to yield reversed cubic phase materials (it being recognized that identification of these amounts is well understood by those of skill in the art—see declaration of Richard Templar) (see claim 66 of the present application). Item 11 of the declaration of David Anderson demonstrates that a minimum amount of spearmint oil is needed for a particular formulation of components to yield reversed cubic phase materials (see claim 67 of the present application).

As noted during the interview, **the use of essential oils creates a four component cubic phase material that yields the surprising and unexpected result that: (i) certain drugs can be brought into reversed cubic phase and reversed hexagonal phase material which could not be, absent the fourth component; and, (ii) increased quantities of otherwise difficult to solubilize drugs can be solubilized in the reversed cubic phase and reversed hexagonal phase material, because of the presence of the fourth component.** As David Anderson explained in a previous declaration, this is because the identified fourth component simultaneously solubilizes the active and modulates the lyotropic liquid crystal phase behavior, this on account of their size and shape and the manner in which they interact with the key structural element of lyotropic liquid crystals, the lipid bilayer. With reference to item 9 of the declaration of David Anderson, it can be seen that increasing amounts of paclitaxel (a difficult to

solubilize drug) can be incorporated in the reversed cubic phase with the addition of essential oils. None of the references of record in the case show or suggest that the use of essential oils or a dissolution/solubilization agent like tocopherol result allow for control of the morphologies of reversed cubic liquid crystalline phases or reversed hexagonal liquid crystalline phases or for increased drug loading in those phases, let alone both at once.

In short, the claims cover a new material, with the important and unobvious advantage of improved drug loading and morphological control. The application describes many variations on these concepts and provides many examples. The declaration evidence in the record shows that combinations proposed by the Examiner do not achieve the claimed invention. The previously filed amendments, and declaratory evidence underscore significant and unobvious differences between the claimed invention and references of record. In view of the important development, and the significant amount of data provided in the application, claims of the breadth proposed are entitled to patent protection.

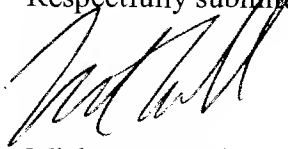
Conclusion

In view of the foregoing, it is requested that the application be reconsidered, that claims 1, 3-27, 29-53, 56, 59, 60, 66, and 67 be allowed, and that the application be passed to issue.

Should the Examiner find the application to be other than in condition for allowance, the Examiner is requested to contact the undersigned at 703-787-9400 (fax: 703-787-7557; email: mike@wcc-ip.com) to discuss any other changes deemed necessary in a telephonic or personal interview.

If an extension of time is required for this response to be considered as being timely filed, a conditional petition is hereby made for such extension of time. Please charge any deficiencies in fees and credit any overpayment of fees to Attorney's Deposit Account No. 50-2041.

Respectfully submitted,

A handwritten signature in black ink, appearing to read "Michael E. Whitham", is written over the typed name.

Michael E. Whitham

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